I. Election

In paragraph 1, the Examiner required election between two groups. The Applicants elect Group I (claims 1-4, 33-60) drawn to a method of diagnosing susceptibility to myocardial infarction or stroke using a haplotype or polymorphism.

At page 3, the Examiner imposed an additional "Sequence Restriction Requirement," alleging that each haplotype and each polymorphism is patentably distinct. In response, the Applicants elect the following combination of markers:

SG13S32, allele A

SG13S114, allele T

The Applicants acknowledge with thanks the Examiner's promise to rejoin combinations that contain the allowable, elected combination. The elected combination of markers are both present in the HapA haplotypes described in the application, and to the extent the Applicants are required to elect a haplotype, they elect HapA, which comprises this combination of markers.

II. Applicants Traverse the Sequence Restriction Requirement

At page 3, the Examiner stated that each sequence is patentably distinct as these sequences are unrelated, for example, the protein encoded by these sequences differ in structure, function and biological activity. The Applicants traverse this restriction because the sequences containing the polymorphisms and haplotypes of the invention are related and do not differ in the manner indicated by the Examiner.

The claims are directed to detecting a polymorphism in the FLAP nucleic acid, or detecting a haplotype in the FLAP nucleic acid. Thus, the markers and/or haplotypes are **related** insofar as they are pertain to the same gene. Generally speaking, the polymorphisms are allelic variations that serve as individual genetic markers, while haplotypes are combinations or sets of genetic markers. The specification defines the term "FLAP nucleic acid" as an isolated nucleic acid encoding the FLAP polypeptide, including non-coding sequences such as introns and non-coding 3' and 5' sequences (see page 14, lines 10-18 of the specification). The full length FLAP nucleic acid is provided as the nucleic acid sequence set out as SEQ ID NO: 1 and the FLAP mRNA/cDNA sequence is provided as SEQ ID NO:

3. The polymorphisms and haplotypes that are recited in the claims are located within the same FLAP nucleic acid sequence. The claimed sequences containing polymorphisms or haplotypes of the invention do not encode different polypeptides as stated by the Examiner. In fact, a large percentage of the polymorphisms are located in the non-coding region of the FLAP gene.

The Examiner also stated that the allelic variations of the invention have different diagnostic and therapeutic implications. However, the elected method claims involve use of polymorphisms and haplotypes to predict risk of the same disease state, susceptibility to myocardial infarction or stroke. The specification provides a number of polymorphisms and haplotypes that correlate with increased risk of myocardial infarction and stroke (see Example 1, *e.g.* pages 81-92). Even though the polymorphisms and haplotypes may correlate with varying degrees of risk for myocardial infarction or stroke, the elected screening methods of using different polymorphisms or haplotypes of the invention are related in their use of FLAP genetic information for diagnosing susceptibility to myocardial infarction or stroke.

The Examiner also stated that the required sequence election is NOT an election of species because the polymorphic nucleic acids are structurally distinct compounds that are unrelated to each other. As described above, the polymorphisms and haplotypes of the invention are within the FLAP nucleic acid set out as SEQ ID NO: 1. The polymorphisms taught in the specification are single nucleotide polymorphisms (SNPs) and therefore by definition these variations only change one nucleotide within the 214,000 nucleotide sequence of SEQ ID NO: 1. The polymorphisms and haplotypes of the invention share a common structural feature (the FLAP gene sequence in which they are found) and share the common utility of predicting the risk for myocardial infarction or stroke. These shared features are required for molecules to be considered "species" of one another and have unity of invention. See M.P.E.P 803.02.

For these reasons, the polymorphisms and haplotypes of the invention should be examined simultaneously. Even if the Examiner maintains the restriction of sequence, this sequence election should be considered an election of species because the polymorphisms and haplotypes share a common structural feature and common utility.

III. The Search of the Claimed Polymophisms and Haplotypes is not Unduly Burdensome

A search based on all the polymorphisms and haplotyeps of the invention would not inflict a serious burden on the Examiner. The M.P.E.P. instructs Examiners that "if a search and examination of an entire application can be made without serious burden, the examiner ***must examine it on its merits even if it includes claims to independent or distinct inventions***." There are two criteria for proper restriction for restriction between patentably distinct inventions:

> (A) The inventions must be independent or distinct as claimed and
>
> (B) There must be a ***serious burden*** on the examiner if restriction is required.

Regardless of whether the claims are limited to the elected markers or all the markers taught in the invention, any search of the invention will involve searching for prior art that correlates FLAP nucleic acid sequence (SEQ ID NO: 1) variations with risk for myocardial infarction or stroke. In other words, the Examiner will undoubtedly search the generic method of the invention along with the elected species. The presence or absence of any number of polymorphisms recited in claims will not alter this aspect of the searching strategy or the number of references identified. Therefore, the initial search burden related to diagnostic use of polymorphisms or haplotypes of the FLAP nucleic acid does not inflict a serious burden on the examiner. Assuming that no significant prior art is found in the search, examination of method claims that recite any combination of FLAP polymorphisms will not pose a significant burden on the Examiner. That is the essence of traditional genus-species restriction practice and examination.

Applicants fail to see how increasing the work load of an examining group by unnecessarily and unreasonably splitting one application into an extremely large number of separate species examinations lessens the burden on the patent office. Such restriction also works tremendous unfairness on the business public. The cost to applicants and competitors of respectively prosecuting analyzing an extremely large number of patents is extremely burdensome, but would be a direct consequence of the Patent Office's restriction policy. In this regard, the Patent Office's own manual warns, in capital letters, that "IT STILL REMAINS IMPORTANT FROM THE STANDPOINT OF THE PUBLIC INTEREST

THAT NO REQUIREMENTS BE MADE WHICH MIGHT RESULT IN THE ISSUANCE OF TWO PATENTS FOR THE SAME INVENTION." (M.P.E.P. 803.01). Because of the large number of predictive haplotypes that the present Applicants have contributed have contributed to the public knowledge, it is grossly unfair to depreive the Applicants of the opportunity for reasonable patent scope simply because one aspect of the search process chosen by the examiner may involve a database search of genetic sequences. Under the current restriction, the number of divisionals required would be cost prohibitive for any applicant to consider.

IV. Location of the Elected Sequences in the Specification

At page 4, the Examiner required that the Applicants distinctly point out the location in the specification to which the elected sequences id drawn. As described above, these polymorphisms are within the FLAP nucleic acid sequence of SEQ ID NO: 1. Table 3 (pages 83-84) provides the genetic location of the elected markers within the NCBI Build 34. The allelic variation of the elected markers is set out in Table 13 at page 98, line2 (SG13S32: A/C) and page 96, line 39 (SG13S114 A/T). The presence and allelic variation of the elected markers within the haplotypes of the invention are set out in Table 5 (pages 84-85), Table 7 (page 87) and Table 9 (pages 89-90).

V. Conclusion

In view of the foregoing remarks, the sequence restriction should be withdrawn, and the polymorphisms and haplotypes of the invention should be examined simultaneously.

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Respectfully submitted,

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